

## CLAIMS

1. A method for detecting the activity of GPR86 in a sample comprising the steps of:

a) incubating a sample comprising GPR86 and ADP under conditions which permit binding of GRP86 and ADP, and

5 b) detecting a second messenger.

2. The method of claim 1 further comprising the steps of:

a) incubating a second sample comprising GPR86 in the absence of ADP under conditions which permit binding of GRP86 and ADP, and

b) detecting a second messenger.

10 3. The method of claim 1 wherein said sample comprises cells expressing GPR86.

4. The method of claim 3 wherein said cells are selected from the group consisting of: COS7-cells, a CHO cell, a LM (TK-) cell, a NIH-3T3 cell, HEK-293 cell, K-562 cell, a 1321N1 astrocytoma cell and other cell lines.

15 5. The method of claim 1 wherein said sample comprises cell membranes bearing GPR86.

6. The method of claim 1, wherein step a) is further performed in the presence of G $\alpha$ 16 polypeptide.

7. A method of screening for a candidate modulator of GPR86 activity using cells expressing GPR86, said method comprising:

20 a) incubating a first sample of said cells in the presence of said candidate modulator and a second sample of said cells in the absence of said candidate modulator, both said samples under conditions which permit binding of ADP to GPR86;

b) detecting a signalling activity of GPR86 polypeptide in said first and second samples, and

c) comparing the results of said second messenger assays for said first and second samples.

8. The method of claim 7 wherein said cell is selected from the group consisting of: COS7-cells, a CHO cell, a LM (TK-) cell, a NIH-3T3 cell, HEK-293 cell, K-562 cell, a 1321NI astrocytoma cell and other cell lines.

9. A method of screening for a candidate modulator of GPR86 activity using cell membranes bearing GPR86, said method comprising:

a) incubating a first sample of said cell membranes in the presence of said candidate modulator and a second sample of said cell membranes in the absence of said candidate modulator, both said samples under conditions which permit binding of ADP to GPR86;

b) detecting a signalling activity of GPR86 polypeptide in said first and second samples, and

c) comparing the results of said second messenger assays for said first and second samples.

10. The methods of claim 7 or 9, further performed in the presence of G $\alpha$  16 polypeptide.

11. A method for determining if a candidate modulator increases or decreases the activity of GPR86 using cells expressing GPR86, said method comprising:

a) incubating a first sample of said cells in the presence of said candidate modulator and a second sample of said cells in the absence of said candidate modulator, both said samples under conditions which permit binding of ADP to GPR86;

b) detecting a signalling activity of GPR86 polypeptide in said first and second samples, and

c) comparing the results of said second messenger assays for said first and second samples.

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12. The method of claim 11 wherein said cells are selected from the group consisting of: COS7-cells, a CHO cell, a LM (TK-) cell, a NIH-3T3 cell, HEK-293 cell, K-562 cell and a 1321N1 astrocytoma cell and other cell lines.

13. A method for determining if a candidate modulator increases or decreases the activity of GPR86 using cell membranes bearing GPR86, said method comprising:

a) incubating a first sample of said cell membranes in the presence of said candidate modulator and a second sample of said cell membranes in the absence of said candidate modulator, both said samples under conditions which permit binding of ADP to GPR86;

b) detecting a signalling activity of GPR86 polypeptide in said first and second samples, and

c) comparing the results of said second messenger assays for said first and second samples.

14. The methods of claim 11 or 13, further performed in the presence of Gα16 polypeptide.

15. A kit for detecting binding to GPR86 or a modulator of GPR86, said kit comprising GPR86 and ADP, and packaging materials therefore, wherein said GPR86 and ADP are packaged separately.

16. The kit of claim 15, wherein GPR86 is present in a cell.

17. The kit of claim 16 wherein said cell is selected from the group consisting of: COS7-cells, a CHO cell, a LM (TK-) cell, a NIH-3T3 cell, HEK-293 cell, K-562 cell and a 1321N1 astrocytoma cell and other cell lines.

18. The kit of claim 15, wherein GPR86 is associated with a cell membrane.

19. The kit of claim 15, said kit further comprising the components of a second messenger assay.

20. The kit of claim 15, wherein the modulator is detected using an antibody specific for GPR86 or a GPR86-specific nucleic acid probe.

21. The kit of claim 15, said kit further comprising Gα16 polypeptide.

22. A non-human mammal comprising a partial or total deletion of the ortholog sequence of the human polynucleotide (SEQ ID NO.1), preferably a non-human mammal comprising a homologous recombinant knockout of said polynucleotide or a transgenic non-human mammal overexpressing above natural level said polynucleotide.

23. A method of identifying an agent that modulates the function of GPR86, said method comprising:

a) contacting a GPR86 polypeptide in the presence and absence of a candidate modulator under conditions permitting the binding of said ADP to said GPR86 polypeptide; and

b) measuring the binding of said GPR86 polypeptide to said candidate modulator, relative to the binding in the absence of said candidate modulator, identifies said candidate modulator as an agent that modulates the function of GPR86.

24. The method of claim 23 wherein said measuring is performed using a method selected from label displacement, surface plasmon resonance, fluorescence resonance energy transfer, fluorescence quenching, and fluorescence polarization.

25. The method of any one of claims 7, 9, 11 and 13 wherein said candidate modulator is selected from the group consisting of a natural or synthetic peptide, a polypeptide, an antibody or antigen-binding fragment thereof, a lipid, a carbohydrate, a nucleic acid, and a small organic molecule.

26. The method of any one of claims 7, 9, 11 and 13 wherein said step of measuring a signalling activity of said GPR86 polypeptide comprises detecting a change in the level of a second messenger.

27. The method of either of claims 7, 9, 11 or 13 wherein the step of detecting a signalling activity comprises measurement of guanine nucleotide binding or exchange, adenylate cyclase activity, cAMP, protein kinase C activity, phosphatidylinositol breakdown,

diacylglycerol, inositol triphosphate, intracellular calcium, arachinoid acid concentration, MAP kinase activity, tyrosine kinase activity, reporter gene expression.

28. The method of claims 27 wherein said measuring a signalling activity comprises using an aequorin-based assay.

5 29. A method of modulating the activity of a GPR86 polypeptide in a cell, said method comprising the step of delivering to said cell an agent that modulates the activity of a GPR86 polypeptide, such that the activity of GPR86 is modulated.

30. A method of diagnosing a disease or disorder characterized by detecting dysregulation of GPR86 signalling, said method comprising:

10 a) contacting a tissue sample with an antibody specific for a GPR86 polypeptide;

b) detecting binding of said antibody to said tissue sample; and

c) comparing the binding detected in step (b) with a standard, wherein a difference in binding relative to said standard is diagnostic of a disease or disorder characterized by dysregulation of GPR86.

15 31. A method of diagnosing a disease or disorder characterized by dysregulation of GPR86 signalling, said method comprising:

a) contacting a tissue sample with an antibody specific for a GPR86 specific ligand;

b) detecting binding of said antibody to said tissue sample; and

20 c) comparing the binding detected in step (b) with a standard, wherein a difference in binding relative to said standard is diagnostic of a disease or disorder characterized by dysregulation of GPR86.

32. A method of diagnosing a disease or disorder characterized by dysregulation of GPR86 signalling, said method comprising:

25 a) contacting a tissue sample with an antibody specific for a GPR86 polypeptide and an antibody specific for a GPR86-specific ligand;

b) detecting binding of said antibodies to said tissue sample; and

c) comparing the binding detected in step (b) with a standard, wherein a difference in the binding of either antibody or both, relative to said standard, is diagnostic of a disease or disorder characterized by dysregulation of GPR86.

5 33. A method of diagnosing a disease or disorder characterized by dysregulation of GPR86 signalling, said method comprising:

a) isolating nucleic acid from a tissue sample;

b) amplifying a GPR86 polynucleotide, using said nucleic acid as a template; and

10 c) comparing the amount of amplified GPR86 polynucleotide produced in step (b) with a standard, wherein a difference in said amount of amplified GPR86 polynucleotide relative to said standard is diagnostic of a disease or disorder characterized by dysregulation of GPR86.

34. A method of diagnosing a disease or disorder characterized by dysregulation of GPR86 signalling, said method comprising:

15 a) isolating nucleic acid from a tissue sample;

b) amplifying a GPR86-specific ligand polynucleotide, using said nucleic acid as a template; and

20 c) comparing the sequence of said amplified GPR86-specific ligand polynucleotide produced in step (b) with a standard, wherein a difference in said sequence, relative to said standard is diagnostic of a disease or disorder characterized by dysregulation of GPR86.

35. The method of claim 33 wherein said GPR86 polynucleotide is SEQ ID NO: 1.

36. The method of claim 33 or 34 wherein said comparing the amount is performed on a microarray.

25 37. An antibody specific for a GPR86 polypeptide.

38. The method of any one of claims 1-6 wherein said incubating is performed in or on virus-induced budding membranes containing a GPR86 polypeptide. A method of detecting the presence, in a sample, of an agent that modulates the function of GPR86, said method comprising:

- 5           a)     contacting a GPR86 polypeptide with said sample;
- b)     measuring a signalling activity of said GPR86 polypeptide in the presence of said sample; and
- c)     comparing said activity measured in the presence of said sample to said activity measured in a reaction in which said GPR86 polypeptide is contacted with a ADP
- 10       present at its  $EC_{50}$ , wherein an agent that modulates the function of GPR86 is detected if the amount of said activity measured in the presence of said sample is at least 50% of the amount induced by said ADP present at it  $EC_{50}$ .

39. A kit for screening for agents that modulate the signalling activity of GPR86, said kit comprising an isolated polynucleotide encoding a GPR86 polypeptide and means for

15       detecting GPR86 signalling, and packaging materials therefore.

40. The kit of claim 39, further comprising the ligand, ADP.

41. A kit for screening for agents that modulate the signalling activity of GPR86, said kit comprising a cell transformed with a polynucleotide encoding a GPR86 polypeptide and means for detecting GPR86 signalling, and packaging materials therefore.

20       42. The kit of claim 39 or 41, wherein the said agents are detected using an antibody specific for GPR86 or a GPR86-specific nucleic acid probe.

43. A kit for the diagnosis of a disease or disorder characterized by dysregulation of GPR86 signalling, said kit comprising an isolated GPR86 polypeptide and means for detecting GPR86 signalling, and packaging materials therefore.

25       44. The kit of claim 43, wherein the said diagnosis or disorder is detected using an antibody specific for GPR86 or a GPR86-specific nucleic acid probe.

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